Proposed Re-evaluation Decision PRVD2010-04

Diodofon

(publié aussi en français)

19 March 2010

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

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Canada

HC Pub: 100113

ISBN: 978-1-100-15149-6 (978-1-100-15150-2)
Catalogue number: H113-27/2010-4E (H113-27/2010-4E-PDF)

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Overview

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the antimicrobial diodofon, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration for the sale and use of products containing diodofon in Canada.

An evaluation of available scientific information found that products containing diodofon do not present unacceptable risks to human health or the environment when used according to the label directions. As a condition of the continued registration of diodofon uses, new risk-reduction measures must be included on the labels of all products. Additional data are being requested as a result of this re-evaluation.

This proposal affects all end-use products containing diodofon registered in Canada. Once the final re-evaluation decision is made, the registrants will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for diodofon and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of diodofon.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health *and* the environment. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

Diodofon, one of the active ingredients in the current re-evaluation cycle, has been re-evaluated under Re-evaluation Program 1. This program relies as much as possible on foreign reviews, typically United States Environmental Protection Agency (USEPA) Reregistration Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, the foreign review must meet the following conditions:

- it covers the main science areas, such as human health and the environment, that are necessary for Canadian re-evaluation decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

Given the outcome of foreign reviews and a review of the chemistry of Canadian products, the PMRA will propose a re-evaluation decision and appropriate risk-reduction measures for Canadian uses of an active ingredient. In this decision, the PMRA takes into account the Canadian use pattern and issues (e.g. the federal Toxic Substances Management Policy [TSMP]).

Based on the health and environmental risk assessments published in a 2008 RED, the USEPA concluded that diodofon was eligible for reregistration provided risk-reduction measures were adopted. The PMRA compared the American and Canadian use patterns and found the USEPA assessments described in this RED were an adequate basis for the proposed Canadian re-evaluation decision.

For more details on the information presented in this overview, please refer to the Science Evaluation section of this consultation document.

What Is Diodofon?

Diodofon is an antimicrobial used as a material preservative in latex paints, pigment dispersions, coatings, latex caulks and adhesives, leather tanning and paper production (wet lap and sheet pulp). Diodofon is handled by professional workers and is added during the manufacturing process of treated articles and materials using open pour or closed systems. Homeowners can use household products which already contain this active ingredient.

Health Considerations

Can Approved Uses of Diodofon Affect Human Health?

Diodofon is unlikely to affect your health when used according to the revised label directions.

People could be exposed to diodofon while working with treated materials during their manufacture or through residential exposure (i.e., homeowners may be exposed during application of the treated product, or postapplication to the treated materials, e.g. paint).

The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

The USEPA concluded that diodofon was unlikely to affect human health provided that risk-reduction measures were implemented. These conclusions apply to the Canadian situation, and equivalent risk-reduction measures are required.

Environmental Considerations

What Happens When Diodofon Is Introduced Into the Environment?

Diodofon is unlikely to affect non-target organisms when used according to the revised label directions.

The USEPA concluded that indoor uses of diodofon were unlikely to affect non-target organisms provided that additional advisory statements to further protect the environment were implemented. These conclusions apply to the Canadian situation.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law. As a result of the re-evaluation of diodofon, the PMRA is proposing further risk-reduction measures for product labels.

Human Health

- Additional protective equipment for handlers
- Removal of uses from wettable powder and dust/powder labels
- Additional advisory label statements indicating that end-use products intended for leather preservation are limited to leather tanning drums only
- Rate reduction for products used in the preservation of exterior latex paints
- Additional advisory label statements prohibiting use in toys or finger paint
- Additional advisory label statements indicating use is for carpet backing only

Environment

- Additional advisory label statements to reduce potential surface and groundwater contamination

What Additional Scientific Information Is Required?

Data are required as a condition of continued registration under section 12 of the *Pest Control Products Act*. The registrants of this active ingredient must provide these data or an acceptable scientific rationale to the PMRA within the timeline specified in the decision letter. Appendix I lists all data requirements.

Next Steps

Before making a final re-evaluation decision on diodofon, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision[2] document that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Science Evaluation

1.0 Introduction

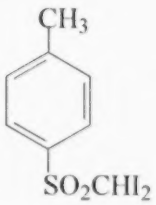
Diodofon is a broad spectrum antimicrobial, algaecide and fungicide.

Following the re-evaluation announcement for diodofon, the registrant of the technical grade active ingredient (a.i.) in Canada indicated that they intended to provide continued support for all uses included on the labels of commercial class end-use products in Canada.

The PMRA used recent assessments of diodofon from the United States Environmental Protection Agency (USEPA). The USEPA Reregistration Eligibility Decision (RED) document for diiodomethyl p-tolyl sulfone (i.e. diodofon), dated 31 March 2008, as well as other information on the regulatory status of diodofon in the United States can be found on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common name	Diodofon
Function	Antimicrobial, Algaecide, Fungicide
Chemical family	Sulfone
Chemical name	
1 **International Union of Pure and Applied Chemistry (IUPAC)**	1-[(diiodomethyl)sulfonyl]-4-methylbenzene diiodomethyl 4-methylphenyl sulfone
2 **Chemical Abstracts Service (CAS)**	Benzene, 1-((diiodomethyl)sulfonyl)-4-methyl-
CAS Registry Number	20018-09-1
Molecular formula	$C_8H_8I_2O_2S$
Structural formula	
Molecular weight	422.02 amu

Purity of the technical grade active ingredient	93.15% minimum
Registration Number	15320

Based on the manufacturing process used, contaminants of human health or environmental concern as identified in the Canada Gazette, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including TSMP Track 1 substances, are not expected to be present in the product.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
UV–visible spectrum	Not expected to absorb at $\lambda > 290$ nm ($\lambda_{max} = 275$ nm)
Solubility in water at 25°C	0.1–1 ppm
***n*-Octanol–water partition coefficient**	*Log* $K_{ow} = 2.66$

2.3 Comparison of Use Patterns in Canada and the United States

Diodofon is an antimicrobial, algaecide and fungicide registered in Canada as a material preservative. It is used in latex paints (exterior and interior), pigment dispersions, coatings, latex caulks and adhesives, leather tanning and in paper production (wet lap and sheet pulp). Commercial class end-use products are formulated as a suspension, wettable powder or dust/powder and have guarantees ranging from 39.2 to 93.15%. They are applied during the manufacturing process of treated materials. The maximum registered concentration in treated materials is 0.6% (by weight) diodofon. Although there are no registered domestic class (i.e. homeowner) diodofon products registered in Canada, there is potential for residential exposure from the use of diodofon-treated products, for example, in paints, caulks and adhesives.

The American and Canadian use patterns were compared. The Canadian formulation types of the end-use products and the uses of diodofon as a material preservative are among those registered in the United States. Based on this comparison of use patterns, it was concluded that the USEPA RED for diodofon was an adequate basis for the re-evaluation of uses of diodofon in Canada.

All current uses are being supported by the registrants and were, therefore, considered in the re-evaluation of diodofon. Appendix II lists all diodofon products that are registered as of 1 November 2009, under the authority of the *Pest Control Products Act*.

3.0 Impact on Human Health and the Environment

In their 2008 RED, the USEPA concluded that the end-use products formulated with diodofon met the safety standard under the American *Federal Insecticide, Fungicide and Rodenticide Act* and would not pose unreasonable risks or adverse effects to humans and the environment if used according to the amended product labels.

3.1 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species.

Exposure to diodofon may occur while working with treated materials during their manufacture, through postapplication exposure to treated materials, or through residential exposure (i.e. homeowners may be exposed during application of the treated product or postapplication to the treated materials such as paint). When assessing health risks, the PMRA considers two key factors: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers).

3.1.1 Occupational Exposure and Risk Assessment

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating safety factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required. The USEPA's toxicological endpoints for assessing risk from occupational exposure are summarized in Appendix III.

Workers can be exposed to diodofon through handling the pesticide or through postapplication exposure to treated materials.

3.1.1.1 Handler Exposure and Risk

Among the exposure scenarios assessed by the USEPA, the following were considered relevant to the Canadian situation:

- Handling liquid for preservation of paper (closed system);
- Handling liquid or wettable powder for preservation of leather (tanning drum; open pour);
- Handling liquid or wettable powder for preservation of paint (open pour);
- Applying paint by a professional painter using a brush/roller or airless sprayer.

Handler exposure analyses were performed using surrogate data from the Pesticide Handlers Exposure Database (PHED) and an antimicrobial study conducted by the Chemical Manufacturers Association, assuming handlers were wearing a long-sleeved shirt, long pants, with and without additional dermal protection (i.e., chemical-resistant gloves) or inhalation protection (i.e., respirator). Dermal and inhalation risks were assessed using maximum concentrations ranging from 0.038 to 0.6% a.i. by weight, or maximum estimated amounts handled ranging from 0.114 to 2.6 kg a.i. per day. In addition, latex paints were considered representative for exposure to latex caulks and adhesives, pigment dispersions and coatings.

Results indicated that occupational exposures and risks were not of concern. Margins of exposure ranged from 104 to 4714 for dermal exposures and 1074 to 4523 for inhalation exposures. For handling wettable powders for preservation of paint, the intermediate-term dermal and the short/intermediate-term inhalation exposures were not of concern for workers wearing chemical-resistant gloves and a respirator. For the professional painter applying paint at rate of 0.3% a.i. with an airless sprayer, short- and intermediate-term dermal and inhalation exposures were not of concern when wearing chemical-resistant gloves.

The RED adequately addressed the potential exposure scenarios associated with the uses of products containing diodofon in Canada, and conclusions apply to the Canadian situation. Based on the risk assessments, the PMRA requires a rate reduction to a maximum of 0.3% a.i. by weight in exterior latex paints and a limitation of wettable powders, dusts and powders to be used only for leather preservation, and only in leather tanning drums. The PMRA also requires long pants, a long-sleeved shirt and chemical-resistant gloves for all formulations including exterior paint applications using an airless sprayer, plus a full face respirator or a half face respirator plus goggles for wettable powder formulations during handling to further protect workers.

The proposed label amendments are listed in Appendix IV.

In addition, the PMRA requires data (similar to US data requests) to refine the dermal and inhalation risk assessments, i.e., a 21/28-day dermal study and a 90-day inhalation study to refine the "professional painter" scenario using airless sprayers; as well as dermal and inhalation exposure data (indoor and outdoor) and use description data to refine the occupational exposure scenarios being supported. These data are required as a condition of continued registration under section 12 of the *Pest Control Products Act*. See Appendix I for the specific data requirements.

3.1.1.2 Postapplication Exposure and Risk

It was determined that potential occupational postapplication exposure to material preservative uses of diodofon was expected to be minimal.

The RED adequately addressed potential exposure associated with the Canadian uses of diodofon as a material preservative, and the USEPA conclusions are applicable to the Canadian situation. Based on this, no mitigation measures are required.

3.1.2 Non-Occupational Exposure and Risk Assessment

3.1.2.1 Residential Exposure

Homeowners can be exposed to diodofon through handling treated products or by coming in contact with treated materials postapplication. Toddlers can be exposed through handling treated material and "hand-to-mouth" activities. The dermal and inhalation endpoints selected by the USEPA for the residential risk assessments were the same as the occupational risk assessments.

The USEPA assessed potential dermal and inhalation short-term exposure and risk to adult handlers from painting with a brush/roller or airless sprayer. Adult handler exposure analyses were performed using surrogate data from PHED, assuming handlers were wearing a short-sleeved shirt and long pants. Results indicated acceptable margins of exposure for handlers applying paint at the reduced rate. Postapplication exposure to bystanders coming into contact with treated paint was expected to be minimal due to the paint being dry and to the low vapour pressure of diodofon. Overall, it was concluded that dermal and inhalation exposures to adult handlers were not of concern.

Toddler exposures and risks were assessed using data from a residue study and surrogate data from the probabilistic Stochastic Human Exposure and Dose Simulation (SHEDS) model. Margins of exposure did not exceed the USEPA's level of concern for short-term dermal and incidental oral exposures to finger paint, nor for short- and intermediate-term dermal and incidental oral exposures for a child contacting a treated surface. The assessment for potential exposure of a child contacting treated carpet (adhesives) concluded that dermal and incidental oral risks would not be of concern since the use of diodofon is for carpet backing only, and not carpet fibres.

The RED adequately addressed the potential exposure scenarios associated with the uses of products containing diodofon in Canada, and conclusions apply to the Canadian situation. Based on this, the PMRA requires a rate reduction to a maximum of 0.3% a.i. by weight in exterior latex paints, as well as additional advisory statements to ensure that end-use products intended for carpet treatment are for carpet-backing use only. In Canada, diodofon is not used in children's toys or finger paints. While such restrictions are not on current labels, the PMRA requires additional advisory statements similar to what is proposed by the USEPA to ensure that diodofon is not incorporated into children's toys or finger paints.

The proposed label amendments are listed in Appendix IV.

In addition, the PMRA requires data (similar to US data requests) to refine the postapplication risk assessment for exposure to painted surfaces, i.e., a dislogeable/transferrable residue study. These data are required as a condition of continued registration under section 12 of the *Pest Control Products Act*. See Appendix I for the specific data requirements.

3.1.2.2 Exposure From Food and Drinking Water

In the United States, diodofon could have indirect contact with food as a result of its use as a material preservative in products used for food packaging or on food contact surfaces, i.e., in adhesives for paper products, in sealants and caulking for repeat use food contact surfaces, and in can side-seam cements. In Canada, there are no food/feed uses of diodofon registered. No acute endpoints of concern were identified by the USEPA and an acute reference dose (RfD) value was not assigned.

A chronic dietary (food) risk assessment was conducted, resulting in exposure of 5 to 33% of the chronic population adjusted dose (cPAD) (or 52% of the cPAD for all exposures combined) for children, the most sensitive subpopulation. The chronic risk assessment was based on "worst-case" dietary concentration values, maximum application rates in treated materials, and the United States Food and Drug Administration's default assumptions.

The USEPA determined that based on the indoor use pattern as a material preservative, diodofon was not expected to have an impact on either surface or groundwater. In Canada, based on diodofon's outdoor use pattern in exterior latex paints, as well as its low solubility in water, it is not expected to reach surface or groundwater.

Overall, the American use pattern encompasses the Canadian use pattern. Considering that treated products could be imported into Canada, the USEPA assessment is considered applicable to the Canadian situation. Based on this, no mitigation measures are required.

3.1.2.3 Aggregate Risk Assessment

Aggregate risk combines the different routes of exposure to diodofon (i.e. from food, water and residential exposures). Short and intermediate-term aggregate risk assessments are comprised of contributions from food, drinking water and non-occupational exposure (dermal, inhalation).

For diodofon, the USEPA short and intermediate-term aggregate risk assessments in children were based on indirect food exposures, handler exposure from finger painting, and postapplication dermal exposure to treated material. Based on the vapour pressure of diodofon, post-application inhalation exposure was expected to be minimal. Dermal and incidental oral aggregate risks were not of concern for each of the exposure scenarios.

Overall, the Canadian aggregate exposure scenarios were adequately addressed by the USEPA aggregate risk assessment. Considering that treated products manufactured in the US could be imported into Canada, the USEPA aggregate exposure conclusions are considered applicable to the uses of diodofon in Canada. No further mitigation measures are required.

3.1.3 Cumulative Effects

The USEPA has not determined whether diodofon has a common mechanism of toxicity with other substances or whether it shares a toxic metabolite produced by other substances. Therefore, it was assumed that diodofon does not share a common mechanism of toxicity with other substances, and a cumulative risk assessment was not required.

3.2 Environment

3.2.1 Environmental Risk Assessment

The USEPA determined that, based on the use pattern, most of the material preservative uses of diodofon were indoors and were to have minimal to no environmental exposure. In the United States, diodofon is also used outdoors as a wood preservative. An outdoor ecological assessment for treated wood was conducted as a "worst-case scenario". It was determined that diodofon has the potential to reach the aquatic environment due to leaching from treated wood. In addition, diodofon was highly to very highly toxic to freshwater fish and invertebrates. Therefore, the USEPA required additional label statements to reduce ecological exposure and further protect non-target organisms.

In Canada, the only outdoor use of material treated with diodofon is exterior latex paints and potential environmental exposure is expected to be minimal. Based on diodofon's low vapour pressure and log *n*-octanol-water partition coefficient (K_{ow}) of 2.66, volatilization and bioaccumulation were not expected to be important fate processes.

Overall, the United States use pattern for diodofon encompasses the Canadian use pattern. Based on the RED, and in consideration of the Canadian situation, the PMRA requires additional advisory label statements to further protect the environment from diodofon discharge. Proposed label amendments are listed in Appendix IV.

3.3 Pest Control Product Policy Considerations

3.3.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances (those that meet all four criteria outlined in the policy, i.e., CEPA-toxic or equivalent, predominantly anthropogenic, persistent and bio-accumulative).

During the reevaluation process, diodofon was assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, and evaluated against the Track 1 criteria for persistence and bioaccumulation. In order for diodofon or its transformation products to meet Track 1 criteria, the criteria for both bioaccumulation and persistence (in one media) must be met.

The log *n*-octanol-water partition coefficient (log K_{ow}) of diodofon is 2.66, which is below the TSMP Track 1 cut-off criterion for log K_{ow} of 5.0. As well, diodofon does not meet the criteria for persistence as its half-life value in soil (1.5 days) is below the TSMP Track 1 cut-off criteria of 182 days. Further, volatilisation is not an important route of dissipation and long-range transport is unlikely based on the vapour pressure (1.87×10^{-6}) and Henry's Law Constant (6.03×10^{-7} atm·m^3/mole). On this basis, it is concluded that the use of diodofon is not expected to result in the entry of Track 1 substances into the environment.

3.3.2 Contaminants and Formulants of Health or Environmental Concern

During the reevaluation of diodofon, contaminants in the technical are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*. The list is used as described in the PMRA Notice of Intent NOI2005-01 and is based on existing policies and regulations including: DIR99-03; and DIR2006-02, and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusion:

- Technical grade diodofon does not contain any contaminants of health or environmental concern identified in the *Canada Gazette.*

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02.

4.0 Incident reports

Starting 26 April 2007, registrants are required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame.

There were no incident reports submitted for diodofon as of 1 November 2009.

5.0 Organisation for Economic Co-operation and Development Status of Diodofon

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups 30 member countries and provides governments with a setting in which to discuss, develop and perfect economic and social policies. They compare experiences, share information and analyses, seek answers to common problems, and work to co-ordinate domestic and international policies to allow for consistency in practices across nations.

Based on the available information, diodofon is permitted for use in the European Union as a slimicide and material preservative in cans, fibre, leather, rubber, polymerised material, masonry and film.

As described earlier in this document, the United States, also an OECD member, assessed the registration of all uses of diodofon in 2008 and concluded using diodofon as a pesticide does not result in unreasonable adverse effects to human health or the environment provided the risk-reduction measures recommended in the RED document were implemented.

The Canadian re-evaluation of diodofon is largely based on the 2008 USEPA assessments. As described in Section 3.1 and 3.2 above, the PMRA has found the USEPA human health and environmental risk conclusions to be relevant to the use of diodofon in Canada and requires measures to mitigate to further protect workers, bystanders and the environment.

6.0 Proposed Re-evaluation Decision

The PMRA has determined that diodofon is acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment. The labels of Canadian end-use products must be amended to include the label statements listed in Appendix IV. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision. The registrant of the technical grade active ingredient is required to submit data as a condition of continued registration under section 12 of the *Pest Control Products Act*. Appendix I lists data requirements.

7.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2001-03, and DACO tables can be found on our website at www.healthcanada.gc.ca/pmra. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra.infoserv@hc-sc.gc.ca.

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxics.

The USEPA RED document for diodofon is available on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

The European Union Directive 98/8/EC on biocidial products is available on the European Commission's webpage at http://ec.europa.eu/environment/biocides/index.htm.

List of Abbreviations

a.i.	active ingredient
amu	atomic mass unit
atm	atmosphere(s)
bw	body weight
°C	degree Celcius
CAS	Chemical Abstracts Service
CEPA	Canadian Environmental Protection Act
cm	centimetre(s)
cPAD	chronic population adjusted dose
DACO	data code
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_{ow}	*n*-octanol–water partition coefficient
m^3	metre(s) cubed
mg	milligram(s)
mm Hg	millimetre mercury
MOE	margin of exposure
NIOSH	National Institute for Occupational Safety and Health
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
PHED	Pesticide Handlers Exposure Database
PMRA	Pest Management Regulatory Agency
ppm	parts per million
PRVD	Proposed Re-evaluation Decision
RED	Reregistration Eligibility Decision
RfD	reference dose
SF	safety factor
TSMP	Toxic Substances Management Policy
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet

Appendix I Additional Data Requirements

The following data are required as a condition of continued registration under section 12 of the *Pest Control Products Act*. The registrants of diodofon are required to provide these data or an acceptable scientific rationale within the timeline specified in the decision letter that will be sent to registrants of the technical active ingredients by the PMRA.

- DACO 4.3.5 Short-term Dermal (21/28-day)
- DACO 4.3.6 Short-term Inhalation (90-day)

  These studies must be conducted with the Canadian technical grade active ingredient or a product with equivalent formulation and guarantee and be conducted according to the appropriate USEPA Office of Prevention Pesticides and Toxic Substances or OECD guidelines.

- DACO 5.2 Use Description/Scenario
- DACO 5.4 Mixer/Loader/Applicator: Passive Dosimetry Data, OR
- DACO 5.11 Glove/Clothing Penetration Data
- DACO 5.9 Dislodgeable/Transferrable Residue

  These studies must be conducted with relevant end-use products and be conducted according to the appropriate USEPA Office of Prevention, Pesticides and Toxic Substances or OECD guidelines.

Appendix II Registered Products Containing Diodofon as of 1 November 2009

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
15320	Technical	Dow Chemical Canada	Amical 48 Antimicrobial Powder	Dust/Powder	93.15
15321	Manufacturing Concentrate and Commercial	Dow Chemical Canada	Amical Flowable Antimicrobial Agent	Suspension	39.2
22910	Commercial	Dow Chemical Canada	Amical WP Antimicrobial Powder	Wettable Powder	47.5
25848	Commercial	Thomson Research Associates	Ultra-Fresh 40	Suspension	39.2
25887	Commercial	Thomson Research Associates	Ultra-Fresh 95	Dust/Powder	93.15
27102	Commercial	Dow Chemical Canada	Amical 48 Antimicrobial Powder A	Dust/Powder	93.15
27475	Commercial	Hercules Canada Inc.	Spectrum PR1912	Suspension	39.2

Appendix III Toxicological Endpoints for Diodofon Health Risk Assessments

Exposure Scenario (route and period of exposure)	Dose (mg/kg bw/day)	Study	Target UF/SF or MOE[a]
Dietary Acute (all populations)	No appropriate endpoints were identified that represent a single dose effect.		
Dietary Chronic (all populations)	Oral NOAEL = 2	90-day oral toxicity study in dogs	UF = 1000 (including 10-fold for database uncertainty) **cPAD = 0.002 mg/kg bw/day**
Incidental Oral short-term (1 – 30 days)	Oral NOAEL = 4	Developmental toxicity study in rabbits	UF = 100 **Target MOE = 100**
Incidental Oral intermediate-term (1 - 6 months)	Oral NOAEL = 2	90-day oral toxicity study in dogs	UF = 100 **Target MOE = 100**
Dermal short-term (1 – 30 days)	Oral NOAEL = 4	Developmental toxicity study in rabbits	UF = 100 **Target MOE = 100**
Dermal intermediate-term (1 – 6 months)	Oral NOAEL = 2	90-day oral toxicity study in dogs	UF = 100 **Target MOE = 100**
Inhalation[b] (all durations)	Oral NOAEL = 2	90-day oral toxicity study in dogs	UF = 100 **Target MOE = 100**
Cancer	Diodofon has not been formally classified for carcinogenicity.		

[a] UF/SF refers to total of uncertainty and/or safety factors for dietary assessments. MOE refers to desired margin of exposure for occupational or residential assessments. The UF of 100 was based on 10× inter-species extrapolation and 10× intra-species variation.

[b] The USEPA considered that for identifying risks of concern the target MOE was 100. However, if results were below a target MOE of 1000, the USEPA considered that confirmatory inhalation toxicity data were warranted. The target MOE of 1000 included a 10-fold SF for route-to-route extrapolation.

NOAEL, no observed adverse effect level.

Appendix IV Label Amendments for Products Containing Diodofon

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the above label statements.

A submission to request label revisions will be required within 90 days of finalization of the re-evaluation decision.

The labels of end-use products in Canada must be amended to include the following statements to further protect workers and the environment.

I) The labels of end-use products formulated as a wettable powder or dust/powder must state on the primary display panel that this product is only to be used for leather tanning drums. All other uses must be removed from product labels.

II) The **DIRECTIONS FOR USE** of the end-use products formulated as suspensions and registered for exterior latex paints must include a maximum application rate of 0.3% (3000 ppm) of active ingredient by weight for all exterior paint uses.

III) The **DIRECTIONS FOR USE** of all end-use product labels must bear clear application rates, e.g., concentrations must indicate if expressed as active ingredient or product concentrations.

IV) The **DIRECTIONS FOR USE** of the labels of all end-use products registered for paint uses must include:

> DO NOT use this product in toys or finger paint.

V) Add to **PRECAUTIONS**:

For end-use products formulated as a wettable powder or dust/powder:

> Wear coveralls over long pants, a long-sleeved shirt, chemical-resistant gloves and footwear, and a full face respirator or a half face respirator plus goggles while cleaning equipment and handling product.

For all other end-use product formulations:

> Wear coveralls over long pants, a long-sleeved shirt, chemical-resistant gloves and footwear, and a face-shield or goggles while cleaning equipment and handling product.

VI) For end-use products registered for exterior latex paints (registration numbers 15321 and 25848), add to the **DIRECTIONS FOR USE**:

> Wear long pants, a long-sleeved shirt and chemical-resistant glove when applying paint with airless sprayers.
>
> It is suggested that the formulator perform field trials within the label rates to determine the best rate for preservation of their paint.
>
> It is recommended to prevent paint chips or dust caused by removing paint from entering water. DO NOT place the painted parts in water after painting until the paint is fully cured.

VII) For adhesives used in carpet treatment, add to the **DIRECTIONS FOR USE**:

> Use only to treat carpet-backing. DO NOT use in carpet fibers.

VIII) For all end-use products, add to the **ENVIRONMENTAL HAZARDS**:

> TOXIC to aquatic organisms. DO NOT discharge effluent containing this product into sewer systems, lakes, streams, ponds, estuaries, oceans or other waters.

References

Studies considered in the Chemistry Assessment

A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

PMRA Document Number	Reference
1250080	CHEMISTRY, DACO: 3 CBI
1789712	DLE-MUJ-2 Amical 48 Preservative Specifications, Method of Manufacture, Product Chemistry, Manufacturing Directions, DACO: 2.1, 2.10, 2.11, 2.13, 2.14.12, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9